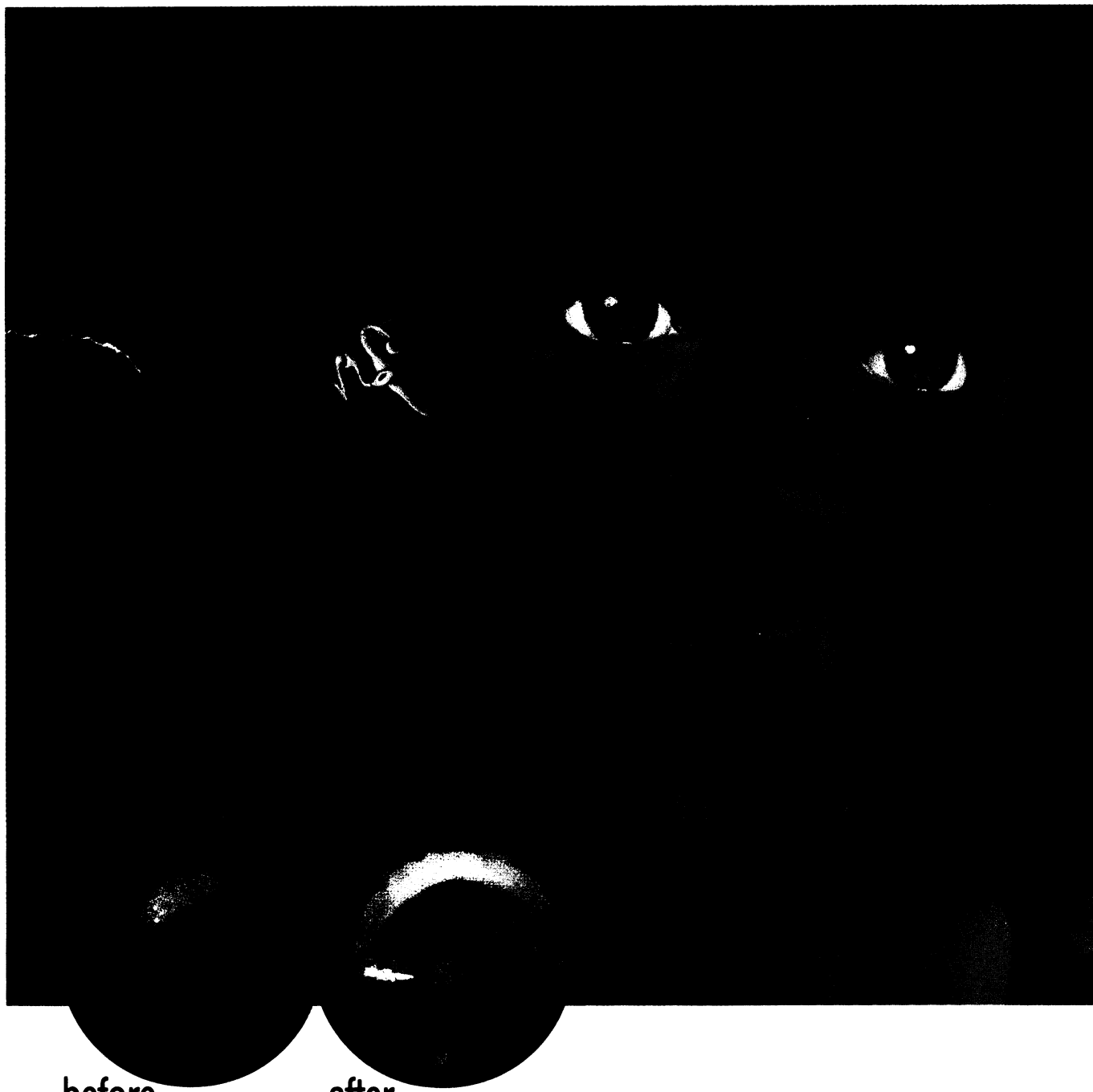
Strong on results.



before Otoscopic view of tympanic membrane in a patient who did not respond to ampicillin

after Same patient after ten days of Bactrim (trimethoprim and sulfamethoxazole/Roche) therapy

Simple to take.

ROCHE®

in acute otitis media

- **Penetrates and clears middle-ear fluid of susceptible strains of *H. influenzae* and *S. pneumoniae*[1]**
- **Reduces evidence of inflammation and bulging eardrum[2]**
- **Results in a reduction of fever, pain and other symptoms[2,3]**

Active against 86% of *H. influenzae in vitro*—even amoxicillin- and ampicillin-resistant strains

Overall, 86% of *Haemophilus influenzae* strains taken from sputum cultures prove susceptible *in vitro* to Bactrim.[4] In one study, 100% of 191 ampicillin-resistant *H. influenzae* isolates were susceptible to Bactrim.[5] However, *in vitro* data do not necessarily correlate with clinical results.

Active against 91% of *S. pneumoniae in vitro*

In sputum cultures of *Streptococcus pneumoniae,* the most frequent pathogen in acute otitis media, 91% of isolates show susceptibility *in vitro* to Bactrim.[4]

Excellent clinical activity—and economical

In comparative clinical trials in children with acute otitis media, Bactrim *b.i.d.* was unsurpassed by ampicillin, amoxicillin or cefaclor.[6]
And the average cost of Bactrim is lower than that of cefaclor and comparable to that of ampicillin and amoxicillin.[7]
Bactrim is indicated in acute otitis media due to susceptible organisms when it offers an advantage over other antimicrobials. Bactrim is contraindicated in pregnancy, lactation, infants under two months of age and documented megaloblastic anemia due to folate deficiency. To date, there are limited data on the safety of repeated use of Bactrim in children under two years of age.

Cherry-flavored suspension

Bactrim™ Pediatric

(trimethoprim and sulfamethoxazole/Roche)

B.I.D. for enhanced compliance.

References: 1. Klimek JJ *et al: J Pediatr* 96:1087-1089. Jun 1980. 2. Schwartz RH *et al: Rev Infect Dis* 4:514-516. Mar-Apr 1982. 3. Cooper J, Inman JS, Dawson AF: *Practitioner* 217:804-809, Nov 1976. 4. Antibiotic Sensitivity Report, Winter 1983. BAC-DATA Medical Information Systems, Inc. 5. Data on file, Hoffmann-La Roche Inc., Nutley, NJ. 6. Wormser GP, Keusch GT, Heel RC: *Drugs* 24:459-518, Dec 1982. 7. *Med Lett Drugs Ther* 23:93-95, Oct 30, 1981.

Please see summary of product information on the following page.

See following page.

Angina comes in many forms...

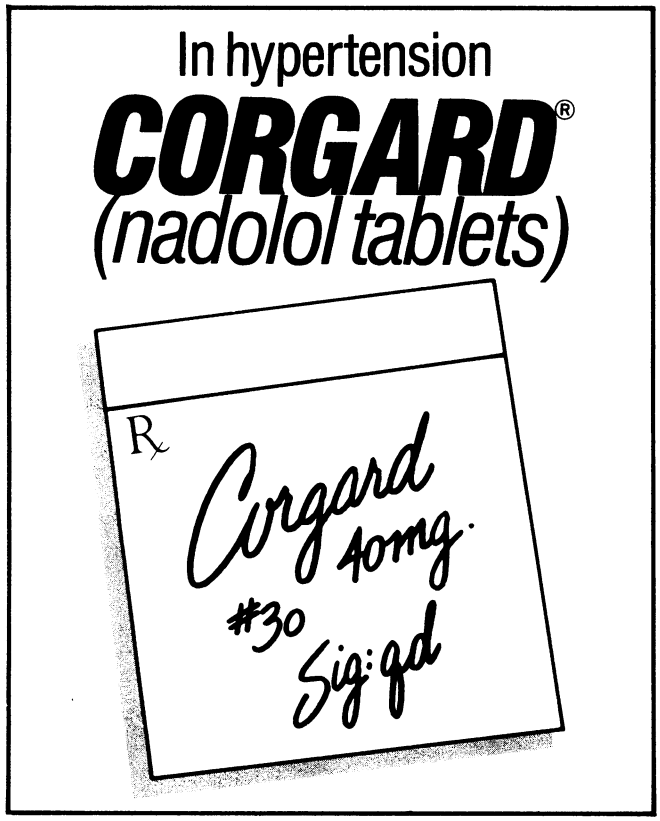
So does

SORBITRATE®

(ISOSORBIDE DINITRATE)

Unsurpassed flexibility in nitrate therapy.

See previous page for brief summary of prescribing information.



CORGARD® TABLETS
Nadolol Tablets

DESCRIPTION: Corgard (nadolol) is a synthetic nonselective beta-adrenergic receptor blocking agent.

CONTRAINDICATIONS: Bronchial asthma, sinus bradycardia and greater than first degree conduction block, cardiogenic shock, and overt cardiac failure (see WARNINGS).

WARNINGS: Cardiac Failure—Sympathetic stimulation may be a vital component supporting circulatory function in congestive heart failure, and its inhibition by beta-blockade may precipitate more severe failure. Although beta-blockers should be avoided in overt congestive heart failure, if necessary, they can be used with caution in patients with a history of failure who are well-compensated, usually with digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle. IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta-blockers can, in some cases, lead to cardiac failure; therefore, at first sign or symptom of heart failure, digitalize and/or give diuretics, and closely observe response or discontinue nadolol (gradually if possible).

Exacerbation of Ischemic Heart Disease Following Abrupt [illegible] Withdrawal—Hypersensitivity to catecholamines has been observed in [illegible] withdrawal of beta-blocker therapy; exacerbation of angina and, in some cases, myocardial infarction have occurred after *abrupt* discontinuation of [illegible] therapy. When discontinuing chronic use of nadolol, particularly in patients with [illegible] gradually reduce dosage over a 1- to 2-week period and carefully monitor the patient. Reinstitute nadolol promptly (at least temporarily) and take other measures appropriate for the management of unstable angina if angina markedly worsens or acute coronary insufficiency develops. Warn patients not to interrupt or discontinue therapy without physician's advice. Because coronary artery disease is common and may be unrecognized, it may be prudent not to discontinue nadolol therapy abruptly even in patients treated only for hypertension.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema)—PATIENTS WITH BRONCHOSPASTIC DISEASE SHOULD IN GENERAL NOT RECEIVE BETA-BLOCKERS. Administer nadolol with caution since it may abolish bronchodilation produced by endogenous or exogenous catecholamine stimulation of $beta_2$ receptors.

Major Surgery—Because beta-blockade impairs the ability of the heart to respond to reflex stimuli and may increase risks of general anesthesia and surgical procedures, resulting in protracted hypotension or low cardiac output, it has generally been suggested that such therapy should be withdrawn several days prior to surgery. Recognition of the increased sensitivity to catecholamines of patients recently withdrawn from beta-blocker therapy, however, has made this recommendation controversial. If possible, withdraw beta-blockers well before surgery takes place. In emergency surgery, inform the anesthesiologist that the patient is on beta-blocker therapy. Use of beta-receptor agonists such as isoproterenol, dopamine, dobutamine, or levarterenol can reverse the effects of nadolol. Difficulty in restarting and maintaining the heart beat has also been reported with beta-adrenergic receptor blocking agents.

Diabetes and Hypoglycemia—Beta-adrenergic blockade may prevent the appearance of premonitory signs and symptoms (e.g., tachycardia and blood pressure changes) of acute hypoglycemia. This is especially important with labile diabetics. Beta-blockade also reduces release of insulin in response to hyperglycemia; therefore, it may be necessary to adjust dose of antidiabetic drugs.

Thyrotoxicosis—Beta-adrenergic blockade may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. To avoid abrupt withdrawal of beta-adrenergic blockade which might precipitate a thyroid storm, carefully manage patients suspected of developing thyrotoxicosis.

PRECAUTIONS: Impaired Renal Function—Use nadolol with caution (see DOSAGE AND ADMINISTRATION section of package insert).

Information for Patients—Warn patients, especially those with evidence of coronary artery insufficiency, against interruption or discontinuation of nadolol without physician's advice. Although cardiac failure rarely occurs in properly selected patients, advise patients being treated with beta-adrenergic blocking agents to consult physician at first sign of impending failure. Advise patients in event of missed doses.

Drug Interactions—Concurrent administration may result in interactions with: Anesthetics, general—exaggeration of the hypotension induced by general anesthetics (see WARNINGS, Major Surgery). Antidiabetic drugs (oral agents and insulin)—hypoglycemia or hyperglycemia; adjust antidiabetic drug dosage accordingly (see WARNINGS, Diabetes and Hypoglycemia). Catecholamine-depleting drugs (e.g., reserpine)—additive effect; monitor closely for hypotension and/or excessive bradycardia.

Carcinogenesis, Mutagenesis, Impairment of Fertility—In 1 to 2 years' oral toxicologic studies in mice, rats, and dogs, nadolol did not produce significant toxic effects. In 2-year oral carcinogenic studies in rats and mice, nadolol did not produce neoplastic, preneoplastic, or nonneoplastic pathologic lesions.

Pregnancy—In animal reproduction studies with nadolol, evidence of embryo-and fetotoxicity was found in rabbits (but not in rats or hamsters) at doses 5 to 10 times greater (on a mg/kg basis) than maximum indicated human dose; no teratogenic potential was seen in any of these species. There are no well-controlled studies in pregnant women; therefore, use nadolol in pregnant women only if potential benefit justifies potential risk to the fetus. Neonates of mothers who received nadolol at parturition have exhibited bradycardia, hypoglycemia and associated symptoms.

Nursing Mothers—Nadolol is excreted in human milk. Exercise caution when nadolol is administered to a nursing woman.

Pediatric Use—Safety and effectiveness in children have not been established.

ADVERSE REACTIONS: Most adverse effects have been mild and transient and have rarely required nadolol withdrawal.

Cardiovascular—Bradycardia with heart rates of less than 60 beats per minute occurs commonly, and heart rates below 40 beats per minute and/or symptomatic bradycardia were seen in about 2 of 100 patients. Symptoms of peripheral vascular insufficiency, usually of the Raynaud type, have occurred in approximately 2 of 100 patients. Cardiac failure, hypotension, and rhythm/conduction disturbances have each occurred in about 1 of 100 patients. Single instances of first degree and third degree heart block have been reported; intensification of AV block is a known effect of beta-blockers (see also CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS). **Central Nervous System**—Dizziness or fatigue reported in approximately 2 of 100 patients; paresthesias, sedation, and change in behavior reported in approximately 6 of 1000 patients. **Respiratory**—Bronchospasm reported in approximately 1 of 1000 patients (see CONTRAINDICATIONS and WARNINGS). **Gastrointestinal**—Nausea, diarrhea, abdominal discomfort, constipation, vomiting, indigestion, anorexia, bloating and flatulence each reported in 1 to 5 of 1000 patients. **Miscellaneous**—Each of the following reported in 1 to 5 of 1000 patients: rash; pruritus; headache; dry mouth, eyes, or skin; impotence or decreased libido; facial swelling; weight gain; slurred speech; cough; nasal stuffiness; sweating; tinnitus; blurred vision; infrequent reversible alopecia. The following adverse reactions have been reported in patients taking nadolol and/or other beta-adrenergic blocking agents, but no causal relationship to nadolol has been established. **Central Nervous System**—reversible mental depression progressing to catatonia; visual disturbances; hallucinations; an acute reversible syndrome characterized by disorientation for time and place; short-term memory loss, emotional lability with slightly clouded sensorium; decreased performance on neuropsychometrics. **Gastrointestinal**—mesenteric arterial thrombosis; ischemic colitis; elevated liver enzymes. **Hematologic**—agranulocytosis; thrombocytopenic or nonthrombocytopenic purpura. **Allergic**—fever combined with aching and sore throat; laryngospasm; respiratory distress. **Miscellaneous**—pemphigoid rash; hypertensive reaction in patients with pheochromocytoma; peculiar disturbances; Peyronie's disease. The oculomucocutaneous syndrome associated with practolol has not been reported with nadolol.

OVERDOSAGE: Nadolol can be removed from the general circulation by hemodialysis. In addition to gastric lavage, employ those forms of treatment as appropriate. In determining duration of corrective therapy, take note of long duration of effect of nadolol.

Excessive bradycardia—Administer atropine (0.25 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.

Cardiac failure—Administer a digitalis glycoside and diuretic. It has been reported that glucagon may also be useful in this situation.

Hypotension—Administer vasopressors, e.g., epinephrine or levarterenol. (There is evidence that epinephrine may be the drug of choice.)

Bronchospasm—Administer a $beta_2$-stimulating agent and/or a theophylline derivative.

DOSAGE: For all patients, DOSAGE MUST BE INDIVIDUALIZED.

For **angina pectoris,** usual initial dose is 40 mg q.d.; may be gradually increased in 40 to 80 mg increments at 3 to 7 day intervals until optimum clinical response or pronounced slowing of the heart rate; usual maintenance dose is 40 or 80 mg q.d. (doses up to 160 or 240 mg daily may be needed). If treatment is to be discontinued, reduce dosage gradually over a period of 1 to 2 weeks (see WARNINGS).

For **hypertension,** usual initial dose is 40 mg q.d.; gradually increase in 40 to 80 mg increments until optimum blood pressure reduction is achieved; usual maintenance dose is 40 or 80 mg q.d. (doses up to 240 or 320 mg daily may be needed).

Patients with renal failure require adjustment in dosing interval; see package insert for dosage in these patients.

For full prescribing information, consult package insert.

HOW SUPPLIED: In scored tablets containing 40, 80, 120, or 160 mg nadolol per tablet in bottles of 100 and in Unimatic® unit-dose packs of 100 tablets. The 40 mg, 80 mg, and 120 mg potencies are also available in bottles of 1000 tablets. (J3-527D)

References: 1. Epstein M, Oster JR: Beta-blockers and the kidney. Min Electrolyte Metab 8:237-254, 1982. 2. Danesh BJZ, et al: Comparison between short-term renal haemodynamic effects of propranolol and nadolol in essential hypertension: a cross-over study. Clin Sci 67:243-248, 1984. 3. Hollenberg NK: Introduction: β-adrenergic blocking agents–the treatment of hypertension and the kidney. Royal Soc of Med Int Congress and Symposium Series 51:1-8, 1982. 4. Frohlich ED, et al: Long-term renal hemodynamic effects of nadolol in patients with essential hypertension. Am Heart J 108:1141-1143, 1984. 5. Alexander JC, et al: Long-term experience with nadolol in treatment of hypertension and angina pectoris. Am Heart J 108:1136-1140, 1984.

PRESERVES RENAL BLOOD FLOW

SQUIBB®
Innovators in cardiovascular medicine

515-542

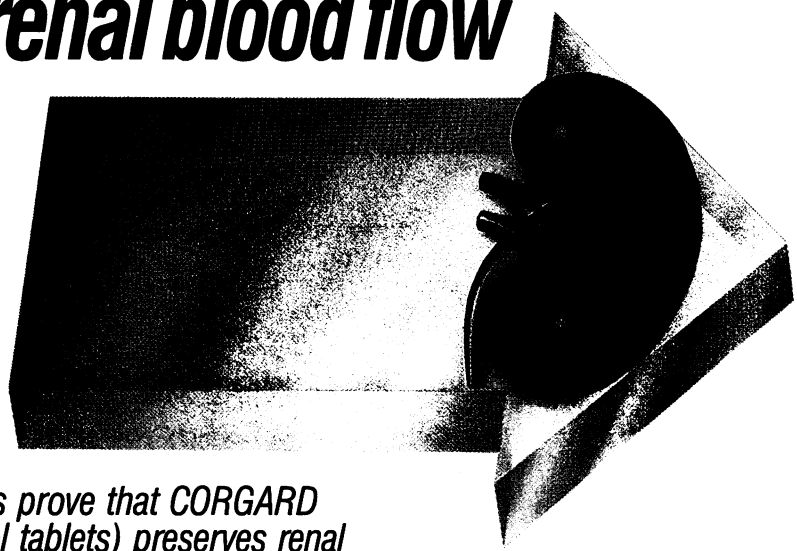
Issued: June 1985

Since with increasing blood pressure there may be a progressive decline in renal blood flow,[1] prescribe . . .

CORGARD® (nadolol tablets)

Lowers blood pressure

Preserves renal blood flow



Studies prove that CORGARD (nadolol tablets) preserves renal blood flow unlike some beta-blockers, such as propranolol.[1-4]

In a two-year study of 106 patients, CORGARD also decreased serum creatinine, a measurement of improved renal function.[5]

- *Offers once-a-day convenience.*
- *Low incidence of CNS side effects.**
- *Avoids potassium depletion.*
- *Maintains long-term control.*

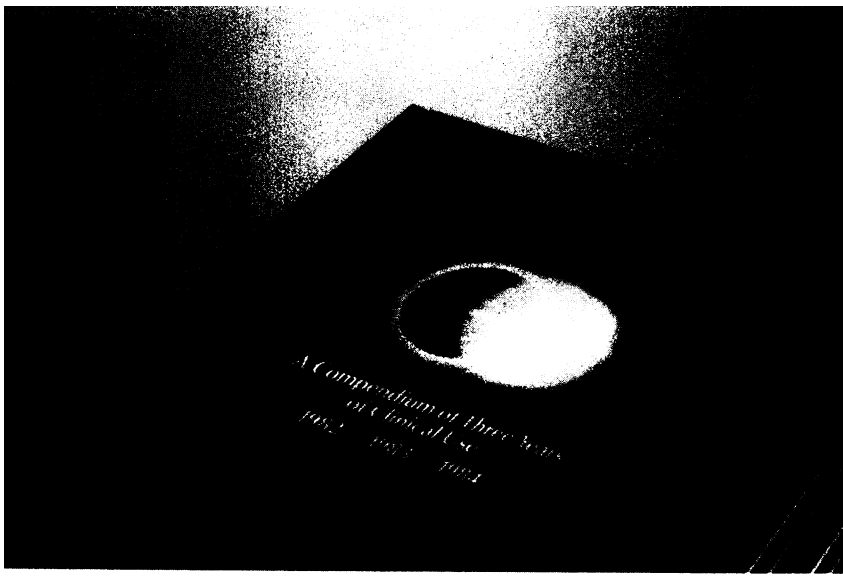
CORGARD®
(nadolol tablets)

STEP-1 FOR HYPERTENSION WITH ONCE-A-DAY DOSE

SQUIBB®

**For a discussion of CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS, and WARNINGS, including avoidance of abrupt withdrawal, please see brief summary of prescribing information on adjacent page.*

a glowing record



a glowing record of acceptance

Desyrel®
(trazodone HCl)

TABLETS: 50 mg, 100 mg, 150 mg

DESCRIPTION

DESYREL® (trazodone hydrochloride) is an antidepressant chemically unrelated to tricyclic, tetracyclic, or other known antidepressant agents. It is a triazolopyridine derivative designated as 2-[3-[4-(3-chlorophenyl)-1-piperazinyl]propyl]-1,2,4-triazolo[4,3-a]pyridin-3-(2H)-one hydrochloride. DESYREL is a white odorless crystalline powder which is freely soluble in water. Its molecular weight is 408.3. The empirical formula is $C_{19}H_{22}ClN_5O \cdot HCl$.

INDICATIONS AND USAGE

DESYREL® (trazodone hydrochloride) is indicated for the treatment of depression. The efficacy of DESYREL has been demonstrated in both inpatient and outpatient settings and for depressed patients with and without prominent anxiety. The depressive illness of patients studied corresponds to the Major Depressive Episode criteria of the American Psychiatric Association's Diagnostic and Statistical Manual, III.[a]

CONTRAINDICATIONS

DESYREL is contraindicated in patients hypersensitive to DESYREL.

WARNINGS

TRAZODONE HAS BEEN ASSOCIATED WITH THE OCCURRENCE OF PRIAPISM. IN APPROXIMATELY ⅓ OF THE CASES REPORTED, SURGICAL INTERVENTION WAS REQUIRED AND, IN A PORTION OF THESE CASES, PERMANENT IMPAIRMENT OF ERECTILE FUNCTION OR IMPOTENCE RESULTED. MALE PATIENTS WITH PROLONGED OR INAPPROPRIATE ERECTIONS SHOULD IMMEDIATELY DISCONTINUE THE DRUG AND CONSULT THEIR PHYSICIAN.

Recent clinical studies in patients with pre-existing cardiac disease indicate that DESYREL may be arrhythmogenic in some patients in that population. Arrhythmias identified include isolated PVCs, ventricular couplets, and in two patients short episodes (3-4 beats) of ventricular tachycardia. Until the results of prospective studies are available, patients with pre-existing cardiac disease should be closely monitored particularly for cardiac arrhythmias. There have also been post-introduction reports of arrhythmias in DESYREL-treated patients, some of whom did not have pre-existing cardiac disease. DESYREL is not recommended for use during the initial recovery phase of myocardial infarction.

PRECAUTIONS

General: The possibility of suicide in seriously depressed patients is inherent in the illness and may persist until significant remission occurs. Therefore, prescriptions should be written for the smallest number of tablets consistent with good patient management. Hypotension, including orthostatic hypotension and syncope, has been reported to occur in patients receiving DESYREL. Concomitant administration of antihypertensive therapy with DESYREL may require a reduction in the dose of the antihypertensive drug. Little is known about the interaction between DESYREL and general anesthetics; therefore, prior to elective surgery, DESYREL should be discontinued for as long as clinically feasible. As with all antidepressants, the use of DESYREL should be based on the consideration of the physician that the expected benefits of therapy outweigh potential risk factors. **Information for Patients:** Alert patients that (a) because priapism has been reported to occur in patients receiving DESYREL, patients with prolonged or inappropriate penile erection should immediately discontinue the drug and consult with the physician; (b) their mental or physical ability to perform potentially hazardous tasks, such as operating machinery or driving, may be impaired; (c) the response to CNS depressants such as alcohol or barbiturates may be enhanced; and (d) DESYREL should be taken shortly after a meal or light snack. **Laboratory Tests:** WBC and differential counts are recommended for patients who develop fever, sore throat or other signs of infection. Discontinue DESYREL if WBC or absolute neutrophil count falls below normal. **Drug Interactions:** Increased serum digoxin or phenytoin levels have been reported to occur in patients receiving DESYREL (trazodone hydrochloride) concurrently with either of those two drugs. Since it is not known whether an interaction will occur between DESYREL and MAO inhibitors, therapy should be initiated cautiously with a gradual increase in dosage until optimum response is achieved, if a MAO inhibitor is discontinued shortly before or is to be given concomitantly with DESYREL. **Therapeutic Interactions:** Concurrent administration with electroshock therapy should be avoided because of the absence of experience in this area. **Carcinogenesis, Mutagenesis, Impairment of Fertility:** No drug- or dose-related occurrence of carcinogenesis was evident in rats receiving DESYREL in daily oral doses up to 300 mg/kg for 18 months. **Pregnancy:** Since there are no adequate and well-controlled studies in pregnant women, DESYREL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Nursing Mothers:** Since DESYREL and/or its metabolites have been found in the milk of lactating rats, caution should be exercised when DESYREL is administered to a nursing woman. **Pediatric Use:** Safety and effectiveness in children below the age of 18 have not been established.

ADVERSE REACTIONS

Clinical Trial Reports: Side effects reported by more than 1% of the patients during clinical trials are the following: **Autonomic**—blurred vision, constipation, dry mouth; **Cardiovascular**—hypertension, hypotension, shortness of breath, syncope, tachycardia/palpitations; **CNS**—anger/hostility, confusion, decreased concentration, disorientation, dizziness/light-headedness, drowsiness, excitement, fatigue, headache, insomnia, impaired memory, nervousness; **Gastrointestinal**—abdominal/gastric distress, bad taste in mouth, diarrhea, nausea/vomiting; **Musculoskeletal**—musculoskeletal aches/pains; **Neurological**—incoordination, paresthesia, tremors; **Sexual Function**—decreased libido; **Skin**—allergic condition/edema; and **Other**—decreased appetite, eyes red/tired/itching, head full-heavy, malaise, nasal/sinus congestion, nightmares/vivid dreams, sweating/clamminess, tinnitus, weight gain, weight loss. Side effects reported by less than 1% of the study patients are the following: akathisia, allergic reaction, anemia, chest pain, delayed urine flow, early menses, flatulence, hallucinations/delusions, hematuria, hypersalivation, hypomania, impaired speech, impotence, increased appetite, increased libido, increased urinary frequency, missed periods, muscle twitches, numbness, and retrograde ejaculation. **Post Introduction Reports:** Voluntary reports received since market introduction include the following: agitation, apnea, diplopia, edema, grand mal seizures, hallucinations, hemolytic anemia, liver enzyme alterations, methemoglobinemia, nausea/vomiting (most frequently), paresthesia, priapism (see PRECAUTIONS, Information for Patients; some patients have required surgical intervention), rash, and weakness. Cardiovascular system effects which have been reported are the following: orthostatic hypotension and syncope, palpitations, bradycardia, atrial fibrillation, myocardial infarction, cardiac arrest, arrhythmia, and ventricular ectopic activity, including ventricular tachycardia (see WARNINGS).

OVERDOSE

Signs and Symptoms: Death from overdose has occurred in patients ingesting DESYREL (trazodone hydrochloride) and other drugs concurrently (namely, alcohol; alcohol + chloral hydrate + diazepam; amobarbital; chlordiazepoxide; or meprobamate). The most severe reactions reported to have occurred with overdose of DESYREL alone have been priapism, respiratory arrest, seizures, and EKG changes. The reactions reported most frequently have been drowsiness and vomiting. Overdosage may cause an increase in incidence or severity of any of the reported adverse reactions (see ADVERSE REACTIONS).

DOSAGE AND ADMINISTRATION

The dosage should be initiated at a low level and increased gradually, noting the clinical response and any evidence of intolerance. Occurrence of drowsiness may require the administration of a major portion of the daily dose at bedtime or a reduction of dosage. DESYREL should be taken shortly after a meal or light snack. **Usual Adult Dosage:** An initial dose of 150 mg/day in divided doses is suggested. The dose may be increased by 50 mg/day every three to four days. The maximum dose for outpatients usually should not exceed 400 mg/day in divided doses. Inpatients may be given up to but not in excess of 600 mg/day in divided doses. **Maintenance:** Dosage during prolonged maintenance therapy should be kept at the lowest effective level. Once an adequate response has been achieved, dosage may be gradually reduced, with subsequent adjustment depending on therapeutic response.

HOW SUPPLIED

DESYREL® (trazodone hydrochloride) 50 mg and 100 mg scored tablets, and 150 mg DIVIDOSE® tablets.

CAUTION: Federal law prohibits dispensing without a prescription.

REFERENCES

a. Williams JBW, Ed: Diagnostic and statistical manual of mental disorders-III, American Psychiatric Association, May 1980.

U.S. Pat. No. 4,215,104

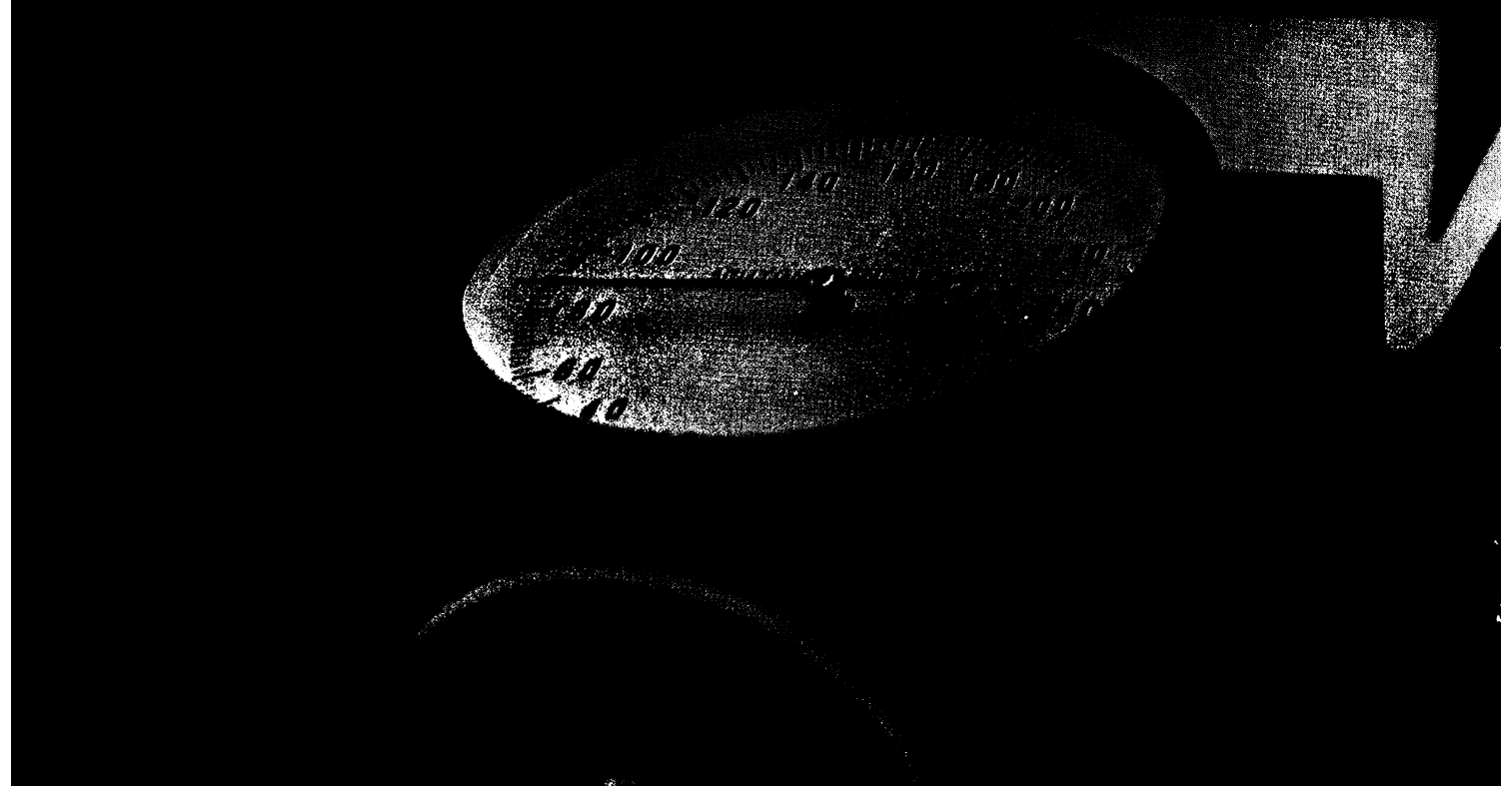
Date of Latest Revision: July 1985

Mead Johnson

PHARMACEUTICAL DIVISION

Mead Johnson & Company • Evansville, Indiana 47721 USA

Right from the start in hypertension...



Once-daily INDERAL LA (propranolol HCl) for smooth blood pressure control without the potassium problems of diuretics

Once-daily INDERAL LA (propranolol HCl) avoids the risk of diuretic-induced ECG abnormalities due to hypokalemia.* In addition, INDERAL LA preserves potassium balance without additive agents or supplements while providing simple, well-tolerated therapy with broad cardiovascular benefits.

Once-daily INDERAL LA for the cardiovascular benefits of the world's leading beta blocker

Simply start with 80 mg once daily. Dosage may be increased to 120 mg to 160 mg once daily as needed to achieve additional control.

Like conventional INDERAL tablets, INDERAL LA should not be used in the presence of congestive heart failure, sinus bradycardia, heart block greater than first degree, and bronchial asthma.

"When it comes to cardiovascular medicine, I like to know exactly what my patients are swallowing."

INDERAL® Tablets

BRAND OF PROPRANOLOL HCl

10 mg 20 mg 40 mg 60 mg 80 mg 90 mg*

BRIEF SUMMARY (FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)

INDERAL® (propranolol hydrochloride) Tablets

CONTRAINDICATIONS

INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

WARNINGS

CARDIAC FAILURE: Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely, or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following abrupt discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned the dosage should be gradually reduced over at least a few weeks and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema)—PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY: The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL, like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, e.g., dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA: Beta-adrenergic blockade may prevent the appearance of certain premonitory signs and symptoms (pulse rate and pressure changes) of acute hypoglycemia in labile insulin-dependent diabetes. In these patients, it may be more difficult to adjust the dosage of insulin.

THYROTOXICOSIS: Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol does not distort thyroid function tests.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS

General: Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL (propranolol hydrochloride) may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

Clinical Laboratory Tests: Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS: Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

Pregnancy: Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose.

There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: INDERAL is excreted in human milk. Caution should be exercised when INDERAL is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular: bradycardia; congestive heart failure; intensification of AV block; hypotension; paresthesia of hands; thrombocytopenic purpura; arterial insufficiency, usually of the Raynaud type.

Central Nervous System: Lightheadedness; mental depression manifested by insomnia, lassitude, weakness, fatigue; reversible mental depression progressing to catatonia; visual disturbances; hallucinations; an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Gastrointestinal: nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic: pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory: bronchospasm.

Hematologic: agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune: In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous: alopecia, LE-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

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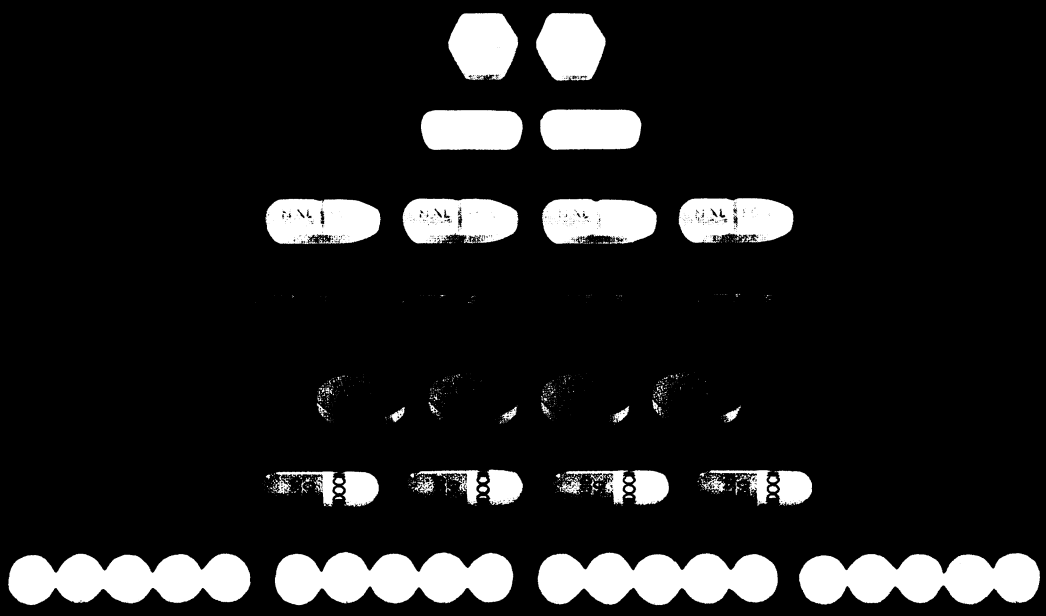

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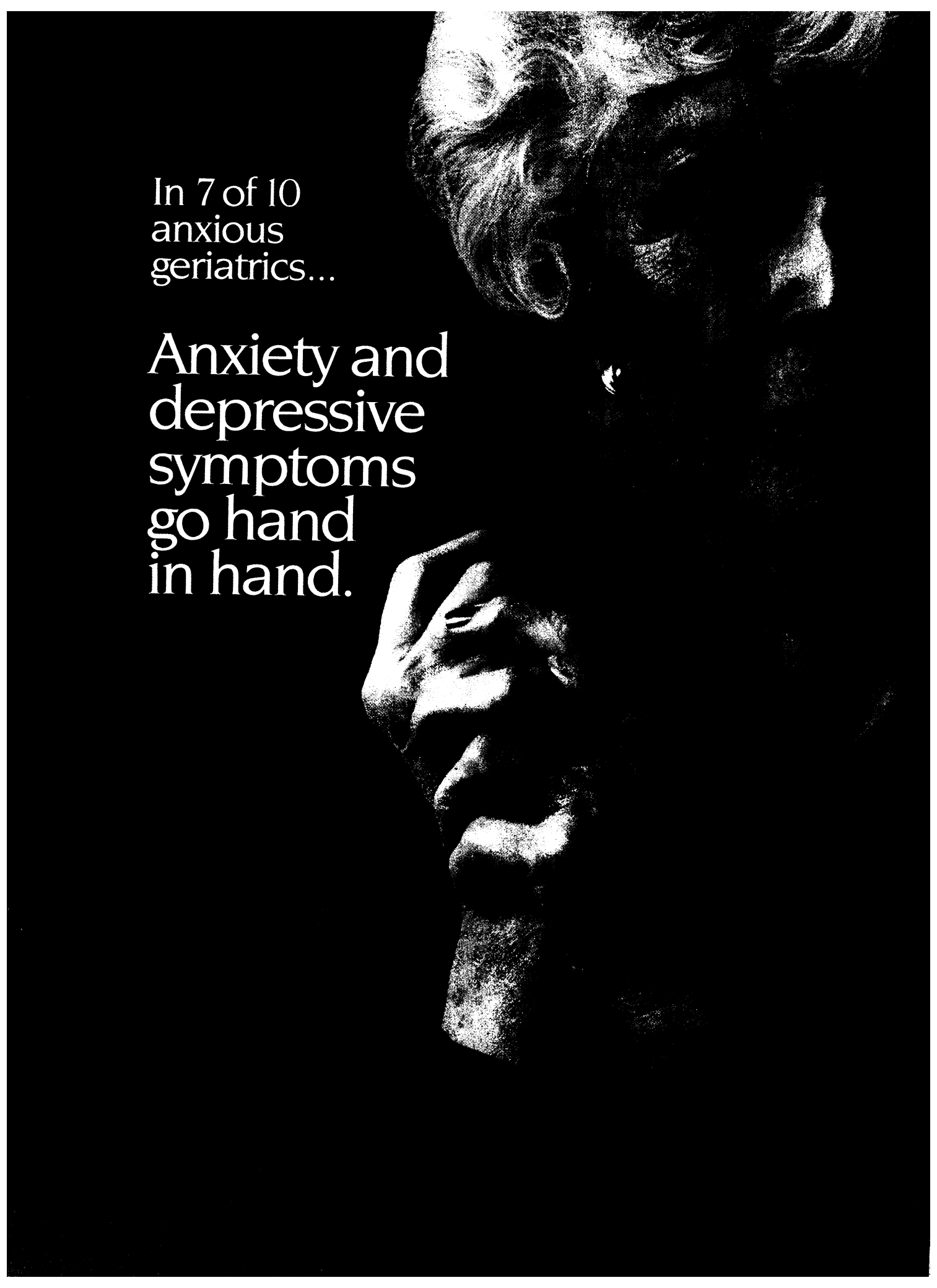
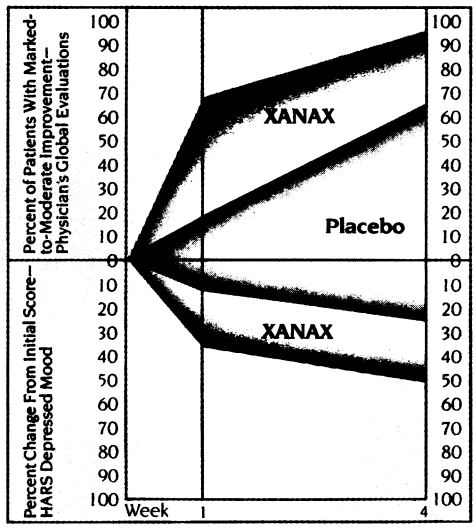

In 7 of 10
anxious
geriatrics...
Anxiety and
depressive
symptoms
go hand
in hand.

Xanax rapidly relieves anxiety with depressive symptoms.



In a recent clinical study[1] of 83 geriatric patients with clinical anxiety, 73% were diagnosed as having symptoms of depressed mood.

XANAX is well suited for therapy because it demonstrates greater efficacy than placebo in reducing the Hamilton Anxiety Rating Scale Total Score and individual items including depressed mood (see Figure).

With clinical advantages for geriatric patients.

- **Rapidly relieves** the symptoms of anxiety
- **Rapidly relieves** associated depressed mood
- **Well tolerated**—mild, transient drowsiness, the most commonly reported side effect the first week of therapy, shows a marked decrease thereafter and is not significantly different from that of placebo
- **Does not cause** cardiotoxicity
- **Specific geriatric dosage**—0.25 mg, two or three times daily

1. Cohn JB: Double-blind safety and efficacy comparison of alprazolam and placebo in the treatment of anxiety in geriatric patients. *Curr Ther Res* 1984;35(1):100-112.

Xanax® 0.25 mg Tablets
alprazolam C-IV

Upjohn THE UPJOHN COMPANY
Kalamazoo, Michigan 49001 USA

Please see next page for brief summary of prescribing information.

WSMA 96th ANNUAL MEETING

WASHINGTON STATE MEDICAL ASSOCIATION

SEPTEMBER 19-22, 1985

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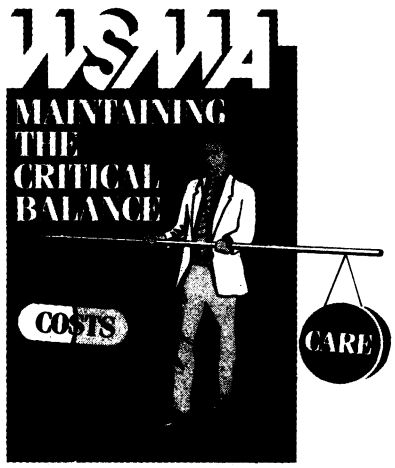


ANNUAL MEETING
SEPTEMBER 19-22, 1985

Annual Meeting Speakers Varied, Provocative

An innovative no-fault approach to tort reform will be presented by Jeffrey O'Connell, professor of law at the University of Virginia. O'Connell specializes in accident and insurance law. He has authored numerous books including a 1979 work, "The Lawsuit Lottery: Only the Lawyers Win." O'Connell will speak to the House of Delegates on Thursday morning, 11:00 a.m.

Harry E. Morgan, Jr, Chairman of the Health Care Purchasers Association of Puget Sound, will also address the House. He will discuss "A Business Prospectus on the Cost of Health Care."

Thursday afternoon Susan M. Schmidt, counsel to the special AMA Task Force on Professional Liability which has produced a series of reports on the issue, will join O'Connell and Morgan on a special reference committee panel. The panel will further review the liability issue and invite physician comment.

Dr Roy M. Schwarz, AMA vice president of medical education and science policy, will address meeting attendees on Friday morning on the future direction of medical education and major science issues facing American medicine in the future.

Meeting Focuses on Change and Challenges

Maintaining the critical balance between costs and care will be an important theme of the 1985 WSMA Annual Meeting. In addition to House of Delegates sessions which will shape future WSMA action on issues, including professional liability, the event-packed four-day meeting will feature a strong social-economic program and comprehensive scientific program.

For further information, please contact:
Washington State Medical Association
2033 Sixth Avenue, #900, Seattle, WA 98121, (206) 441-9762

"When the Ayerst rep told me it costs about 45¢ a day, I said you can stop right there."

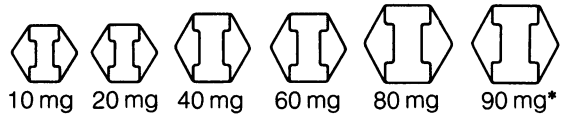
Most doctors are pleasantly surprised to learn that the average cost of daily therapy with the world's most widely used beta blocker is so little, not much more than the cost of a daily newspaper.

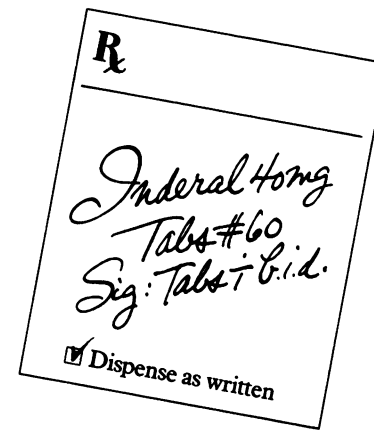
When it's INDERAL (propranolol hydrochloride) tablets you want for your hypertension patients, remember to specify Dispense As Written (DAW) or Do Not Substitute on your prescriptions. That way, you can always be assured they'll get INDERAL®. Please see next page for brief summary of prescribing information.

INDERAL®
(PROPRANOLOL HCl)
Small price to pay.

"When the Ayerst rep told me it costs about 45¢ a day, I said you can stop right there."

INDERAL® TABLETS
(PROPRANOLOL HCl)





BRIEF SUMMARY (FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)

INDERAL® (propranolol hydrochloride) Tablets

CONTRAINDICATIONS

INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

WARNINGS

CARDIAC FAILURE: Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely, or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following abrupt discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned the dosage should be gradually reduced over at least a few weeks and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema)—PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY: The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL, like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, e.g., dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA: Beta-adrenergic blockade may prevent the appearance of certain premonitory signs and symptoms (pulse rate and pressure changes) of acute hypoglycemia in labile insulin-dependent diabetes. In these patients, it may be more difficult to adjust the dosage of insulin.

THYROTOXICOSIS: Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol does not distort thyroid function tests.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS

General: Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL (propranolol hydrochloride) may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

Clinical Laboratory Tests: Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS: Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

Pregnancy: Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose.

There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: INDERAL is excreted in human milk. Caution should be exercised when INDERAL is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular: bradycardia; congestive heart failure; intensification of AV block; hypotension; paresthesia of hands; thrombocytopenic purpura; arterial insufficiency, usually of the Raynaud type.

Central Nervous System: Lightheadedness; mental depression manifested by insomnia, lassitude, weakness, fatigue; reversible mental depression progressing to catatonia; visual disturbances; hallucinations; an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Gastrointestinal: nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic: pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory: bronchospasm.

Hematologic: agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

Auto-Immune: In extremely rare instances, systemic lupus erythematosus has been reported.

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Extra-Strength Motrin Tablets— a convenient way to tap the full potential of Motrin:

The newest strength of *Motrin* Tablets

makes treatment easier for arthritis patients who need the doses that provide higher levels of anti-inflammatory activity as well as potent analgesia...just 1 tablet t.i.d. provides 2400 mg/day.

expands the dosage convenience of MOTRIN Tablets—makes it even easier to adjust the dosage of MOTRIN to each patient's needs...the new dosage range of up to 3200 mg/day can be achieved on a q.i.d. regimen. Gastroscopic studies at varying doses show an increased tendency toward gastric irritation at higher doses. However, at comparable doses, gastric irritation is about half that seen with aspirin.

provides economy...patients should pay less for MOTRIN Tablets than comparable dosages of Clinoril, Feldene, or Naprosyn.

provides, above all, the experience-proven efficacy and safety profile of *Motrin.* MOTRIN continues to be America's most often prescribed nonsteroidal anti-inflammatory agent.

Please turn the page for a brief summary of prescribing information.

Upjohn

The Upjohn Company, Kalamazoo, Michigan 49001

Before prescribing, see complete prescribing information in SK&F CO. literature or *PDR*. The following is a brief summary.

★ **WARNING**

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K^+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K^+ intake. **Associated widened QRS complex or arrhythmia requires prompt additional therapy.** Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.

Precautions: The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically, a patient transferred from the single entities of Dyrenium (triamterene, SK&F CO.) and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin [ACTH]). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function. They can precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, 'Dyazide' should be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine. Hypokalemia is uncommon with 'Dyazide', but should it develop, corrective measures should be taken such as potassium supplementation or increased dietary intake of potassium-rich foods. Corrective measures should be instituted cautiously and serum potassium levels determined. Discontinue corrective measures and 'Dyazide' should laboratory values reveal elevated serum potassium. Chloride deficit may occur as well as dilutional hyponatremia. Concurrent use with chlorpropamide may increase the risk of severe hyponatremia. Serum PBI levels may decrease without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. 'Dyazide' should be withdrawn before conducting tests for parathyroid function.

Thiazides may add to or potentiate the action of other antihypertensive drugs.

Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on 'Dyazide', although a causal relationship has not been established.

Supplied: 'Dyazide' is supplied as a red and white capsule, in bottles of 1000 capsules; Single Unit Packages (unit-dose) of 100 (intended for institutional use only); in Patient-Pak™ unit-of-use bottles of 100.

BRS-DZ:L39

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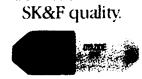
The unique red and white Dyazide® capsule: Your assurance of SK&F quality.

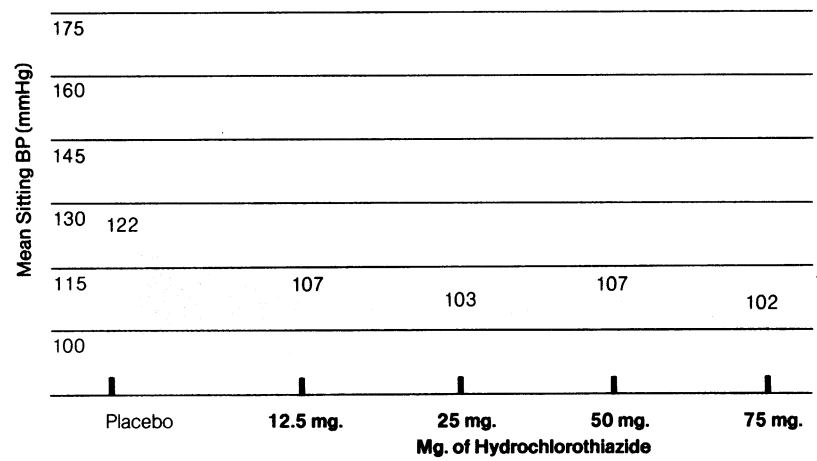


The Benefits of Less

Low doses of hydrochlorothiazide can provide most of the antihypertensive effect of larger doses.[1]

Increasing dosage above 25 mg. daily or improving bioavailability will not lead to increased antihypertensive efficacy in the majority of patients, but can result in a higher incidence of hypokalemia, hyperuricemia and hyperglycemia.[2]

HYDROCHLOROTHIAZIDE: FLAT DOSE-RESPONSE CURVE[3]



For the benefits of low dose diuretic therapy* with the added benefit of potassium-sparing triamterene

PRESCRIBE

DYAZIDE®

25 mg Hydrochlorothiazide/**50 mg** Triamterene/SKF

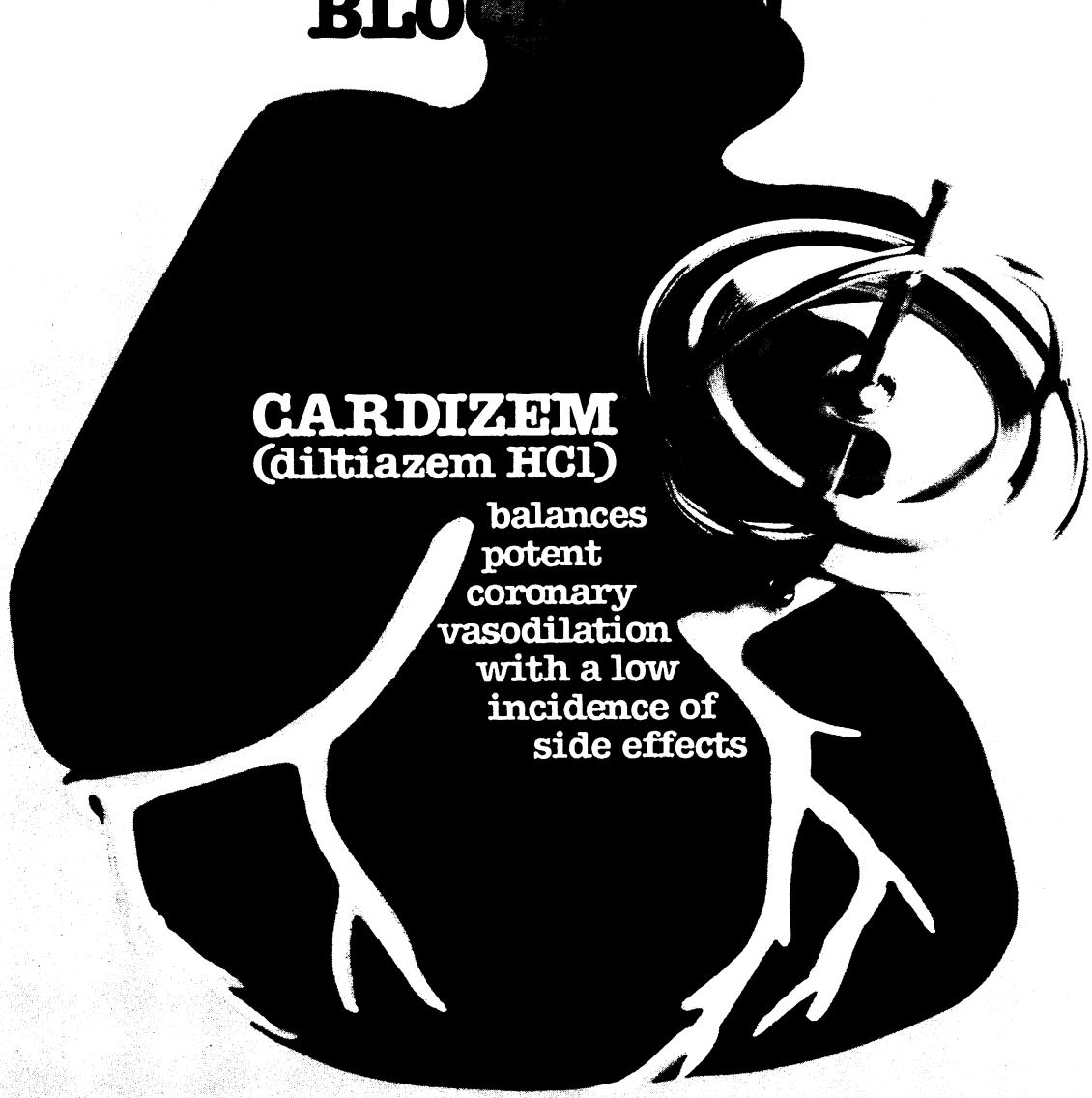
*Not for initial therapy. See boxed warning.

1. Kaplan, N.: Systemic Hypertension: Therapy, in Braunwald, E. (ed.), Heart Disease. A Textbook of Cardiovascular Medicine, Philadelphia, W.B. Saunders Co., vol. 1, pp. 922-951.

2. Dialogues in Hypertension, Hypertension Update II: New Developments in Antihypertensive Therapy, Jan. 1985, Health Learning Systems Inc.

3. Adapted from Beerman, B., and Groschinsky-Grind, M.: Antihypertensive Effect of Various Doses of Hydrochlorothiazide and Its Relation to the Plasma Level of the Drug, Eur. J. Clin. Pharmacol. 13: 195-201, 1978.

BALANCED CALCIUM CHANNEL BLOCKER



Low incidence of side effects
CARDIZEM® (diltiazem HCl) produces an incidence of adverse reactions not greater than that reported with placebo therapy, thus contributing to the patient's sense of well-being.

*Cardizem is indicated in the treatment of angina pectoris due to coronary artery spasm and in the management of chronic stable angina (classic effort-associated angina) in patients who cannot tolerate therapy with beta-blockers and/or nitrates or who remain symptomatic despite adequate doses of these agents.

References:
1. Strauss WE, McIntyre KM, Parisi AF, et al: Safety and efficacy of diltiazem hydrochloride for the treatment of stable angina pectoris: Report of a cooperative clinical trial. Am J Cardiol 49:660-666, 1982.
2. Ford PE, Seagren SC, Bonanno JA, et al: The treatment of exercise-inducible chronic stable angina with diltiazem: Effect on treadmill exercise. Chest 78 (July suppl):234-238, 1980.

Reduces angina attack frequency*
42% to 46% decrease reported in multicenter study.[1]

Increases exercise tolerance*
In Bruce exercise test,[2] control patients averaged 8.0 minutes to onset of pain; Cardizem patients averaged 9.8 minutes ($P<.005$).

CARDIZEM®
(diltiazem HCl)

THE BALANCED CALCIUM CHANNEL BLOCKER

Please see full prescribing information on following page.

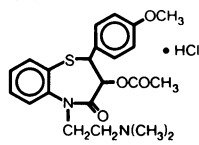
2/84

PROFESSIONAL USE INFORMATION

Cardizem®
(diltiazem HCl)
30 mg and 60 mg tablets

DESCRIPTION

CARDIZEM® (diltiazem hydrochloride) is a calcium ion influx inhibitor (slow channel blocker or calcium antagonist). Chemically, diltiazem hydrochloride is 1,5-Benzothiazepin-4(5H)one,3-(acetyloxy) -5-[2-(dimethylamino)ethyl]-2,3-dihydro-2-(4-methoxyphenyl)-, monohydrochloride,(+) -cis-. The chemical structure is:



Diltiazem hydrochloride is a white to off-white crystalline powder with a bitter taste. It is soluble in water, methanol, and chloroform. It has a molecular weight of 450.98. Each tablet of CARDIZEM contains either 30 mg or 60 mg diltiazem hydrochloride for oral administration.

CLINICAL PHARMACOLOGY

The therapeutic benefits achieved with CARDIZEM are believed to be related to its ability to inhibit the influx of calcium ions during membrane depolarization of cardiac and vascular smooth muscle.

Mechanisms of Action. Although precise mechanisms of its antianginal actions are still being delineated, CARDIZEM is believed to act in the following ways:

1. Angina Due to Coronary Artery Spasm: CARDIZEM has been shown to be a potent dilator of coronary arteries both epicardial and subendocardial. Spontaneous and ergonovine-induced coronary artery spasm are inhibited by CARDIZEM.
2. Exertional Angina: CARDIZEM has been shown to produce increases in exercise tolerance, probably due to its ability to reduce myocardial oxygen demand. This is accomplished via reductions in heart rate and systemic blood pressure at submaximal and maximal exercise work loads.

In animal models, diltiazem interferes with the slow inward (depolarizing) current in excitable tissue. It causes excitation-contraction uncoupling in various myocardial tissues without changes in the configuration of the action potential. Diltiazem produces relaxation of coronary vascular smooth muscle and dilation of both large and small coronary arteries at drug levels which cause little or no negative inotropic effect. The resultant increases in coronary blood flow (epicardial and subendocardial) occur in ischemic and nonischemic models and are accompanied by dose-dependent decreases in systemic blood pressure and decreases in peripheral resistance.

Hemodynamic and Electrophysiologic Effects. Like other calcium antagonists, diltiazem decreases sinoatrial and atrioventricular conduction in isolated tissues and has a negative inotropic effect in isolated preparations. In the intact animal, prolongation of the AH interval can be seen at higher doses.

In man, diltiazem prevents spontaneous and ergonovine-provoked coronary artery spasm. It causes a decrease in peripheral vascular resistance and a modest fall in blood pressure and, in exercise tolerance studies in patients with ischemic heart disease, reduces the heart rate-blood pressure product for any given work load. Studies to date, primarily in patients with good ventricular function, have not revealed evidence of a negative inotropic effect; cardiac output, ejection fraction, and left ventricular end diastolic pressure have not been affected. There are as yet few data on the interaction of diltiazem and beta-blockers. Resting heart rate is usually unchanged or slightly reduced by diltiazem.

Intravenous diltiazem in doses of 20 mg prolongs AH conduction time and AV node functional and effective refractory periods approximately 20%. In a study involving single oral doses of 300 mg of CARDIZEM in six normal volunteers, the average maximum PR prolongation was 14% with no instances of greater than first-degree AV block. Diltiazem-associated prolongation of the AH interval is not more pronounced in patients with first-degree heart block. In patients with sick sinus syndrome, diltiazem significantly prolongs sinus cycle length (up to 50% in some cases).

Chronic oral administration of CARDIZEM in doses of up to 240 mg/day has resulted in small increases in PR interval, but has not usually produced abnormal prolongation. There were, however, three instances of second-degree AV block and one instance of third-degree AV block in a group of 959 chronically treated patients.

Pharmacokinetics and Metabolism. Diltiazem is absorbed from the tablet formulation to about 80% of a reference capsule and is subject to an extensive first-pass effect, giving an absolute bioavailability (compared to intravenous dosing) of about 40%. CARDIZEM undergoes extensive hepatic metabolism in which 2% to 4% of the unchanged drug appears in the urine. In vitro binding studies show CARDIZEM is 70% to 80% bound to plasma proteins. Competitive ligand binding studies have also shown CARDIZEM binding is not altered by therapeutic concentrations of digoxin, hydrochlorothiazide, phenylbutazone, propranolol, salicylic acid, or warfarin. Single oral doses of 30 to 120 mg of CARDIZEM result in detectable plasma levels within 30 to 60 minutes and peak plasma levels two to three hours after drug administration. The plasma elimination half-life following single or multiple drug administration is approximately 3.5 hours. Desacetyl diltiazem is also present in the plasma at levels of 10% to 20% of the parent drug and is 25% to 50% as potent a coronary vasodilator as diltiazem. Therapeutic blood levels of CARDIZEM appear to be in the range of 50 to 200 ng/ml. There is a departure from dose-linearity when single doses above 60 mg are given; a 120-mg dose gave blood levels three times that of the 60-mg dose. There is no information about the effect of renal or hepatic impairment on excretion or metabolism of diltiazem.

INDICATIONS AND USAGE

1. **Angina Pectoris Due to Coronary Artery Spasm.** CARDIZEM is indicated in the treatment of angina pectoris due to coronary artery spasm. CARDIZEM has been shown effective in the treatment of spontaneous coronary artery spasm presenting as Prinzmetal's variant angina (resting angina with ST-segment elevation occurring during attacks).
2. **Chronic Stable Angina (Classic Effort-Associated Angina).** CARDIZEM is indicated in the management of chronic stable angina. CARDIZEM has been effective in controlled trials in reducing angina frequency and increasing exercise tolerance.

There are no controlled studies of the effectiveness of the concomitant use of diltiazem and beta-blockers or of the safety of this combination in patients with impaired ventricular function or conduction abnormalities.

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, patients receiving CARDIZEM have exhibited reversible acute hepatic injury as evidenced by moderate to extreme elevations of liver enzymes. (See PRECAUTIONS and ADVERSE REACTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS).

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, exercise caution when CARDIZEM is administered to a nursing woman if the drug's benefits are thought to outweigh its potential risks in this situation.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences, as well as their frequency of presentation, are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%), AV block (1.1%). In addition, the following events were reported infrequently (less than 1%) with the order of presentation corresponding to the relative frequency of occurrence.

Cardiovascular:	Flushing, arrhythmia, hypotension, bradycardia, palpitations, congestive heart failure, syncope.
Nervous System:	Paresthesia, nervousness, somnolence, tremor, insomnia, hallucinations, and amnesia.
Gastrointestinal:	Constipation, dyspepsia, diarrhea, vomiting, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH.
Dermatologic:	Pruritus, petechiae, urticaria, photosensitivity.
Other:	Polyuria, nocturia.

The following additional experiences have been noted:

A patient with Prinzmetal's angina experiencing episodes of vasospastic angina developed periods of transient asymptomatic asystole approximately five hours after receiving a single 60-mg dose of CARDIZEM.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: erythema multiforme; leukopenia; and extreme elevations of alkaline phosphatase, SGOT, SGPT, LDH, and CPK. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

OVERDOSAGE OR EXAGGERATED RESPONSE

Overdosage experience with oral diltiazem has been limited. Single oral doses of 300 mg of CARDIZEM have been well tolerated by healthy volunteers. In the event of overdosage or exaggerated response, appropriate supportive measures should be employed in addition to gastric lavage. The following measures may be considered:

Bradycardia	Administer atropine (0.60 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.
High-Degree AV Block	Treat as for bradycardia above. Fixed high-degree AV block should be treated with cardiac pacing.
Cardiac Failure	Administer inotropic agents (isoproterenol, dopamine, or dobutamine) and diuretics.
Hypotension	Vasopressors (eg, dopamine or levarterenol bitartrate).

Actual treatment and dosage should depend on the severity of the clinical situation and the judgment and experience of the treating physician.

The oral/LD_{50}'s in mice and rats range from 415 to 740 mg/kg and from 560 to 810 mg/kg, respectively. The intravenous LD_{50}s in these species were 60 and 38 mg/kg, respectively. The oral LD_{50} in dogs is considered to be in excess of 50 mg/kg, while lethality was seen in monkeys at 360 mg/kg. The toxic dose in man is not known, but blood levels in excess of 800 ng/ml have not been associated with toxicity.

DOSAGE AND ADMINISTRATION

Exertional Angina Pectoris Due to Atherosclerotic Coronary Artery Disease or Angina Pectoris at Rest Due to Coronary Artery Spasm. Dosage must be adjusted to each patient's needs. Starting with 30 mg four times daily, before meals and at bedtime, dosage should be increased gradually (given in divided doses three or four times daily) at one- to two-day intervals until optimum response is obtained. Although individual patients may respond to any dosage level, the average optimum dosage range appears to be 180 to 240 mg/day. There are no available data concerning dosage requirements in patients with impaired renal or hepatic function. If the drug must be used in such patients, titration should be carried out with particular caution.

Concomitant Use With Other Antianginal Agents:

1. **Sublingual NTG** may be taken as required to abort acute anginal attacks during CARDIZEM therapy.
2. **Prophylactic Nitrate Therapy**—CARDIZEM may be safely coadministered with short- and long-acting nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.
3. **Beta-blockers.** (See WARNINGS and PRECAUTIONS.)

HOW SUPPLIED

Cardizem 30-mg tablets are supplied in bottles of 100 (NDC 0088-1771-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1771-49). Each green tablet is engraved with MARION on one side and 1771 engraved on the other. CARDIZEM 60-mg scored tablets are supplied in bottles of 100 (NDC 0088-1772-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1772-49). Each yellow tablet is engraved with MARION on one side and 1772 on the other.

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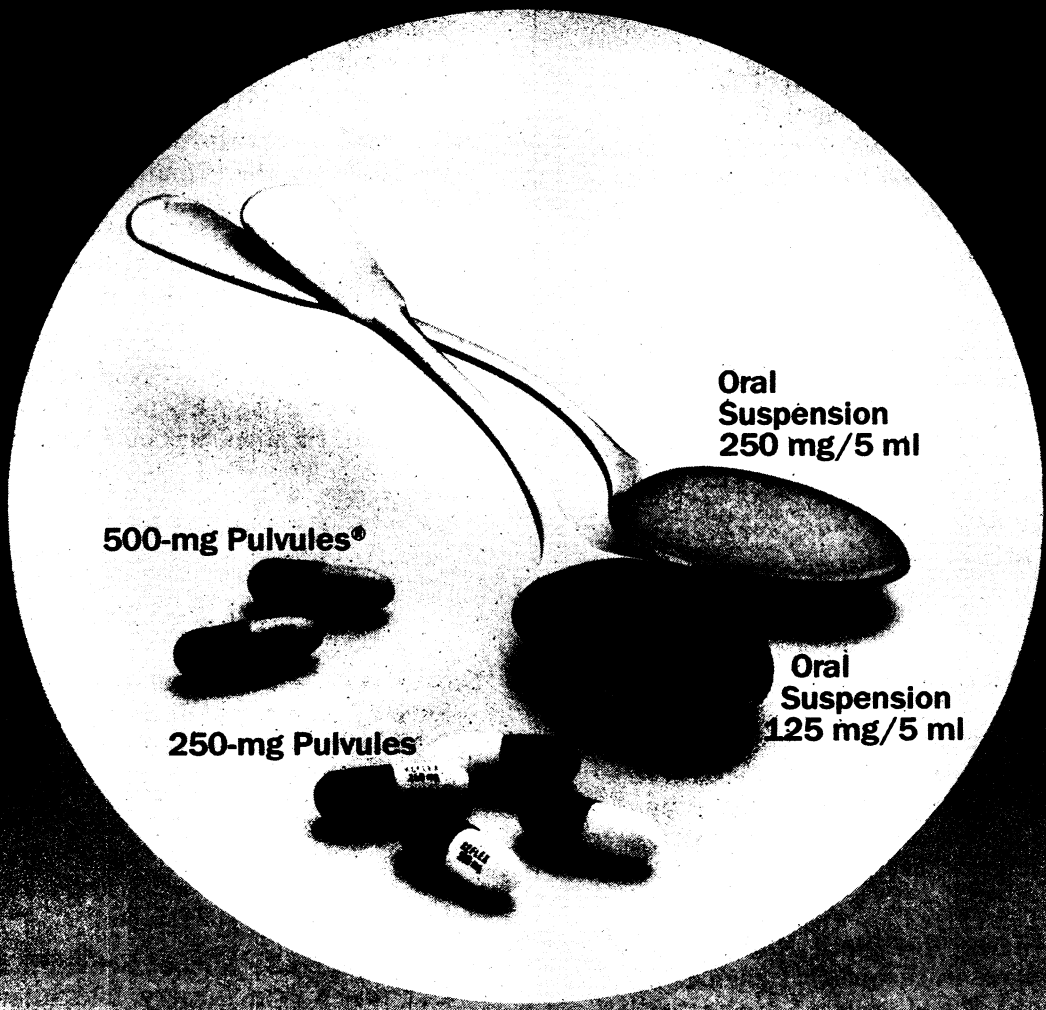

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Westin Hotel Utah, Salt Lake City
September 25-27, 1985

Forum on Medical Issues Thursday, September 26, 1985 2:00-5:00 p.m.

Government

Carolyne K. Davis, RN, PhD
Administrator of the Health Care Financing Administration (HCFA), Dr Davis oversees the functions of the Medicare and Medicaid programs. HCFA helps to finance health care services for 50 million poor, elderly and disabled Americans with a budget over $90 billion in fiscal year 1985.

Medical Ethics

Ernlé W. D. Young, PhD
Chaplain at the Stanford University Medical Center, Dr Young is a senior lecturer on medical ethics. With a worldwide perspective, Dr Young is well informed on ethical conflicts currently facing medicine.

Hospitals

Scott S. Parker, MHA
Executive officer and president for Intermountain Health Care, Mr Parker is also chairman of the Board of Trustees for the American Hospital Association and past chairman of Associated Health Systems.

Physicians

Joseph F. Boyle, MD
Immediate past president of the American Medical Association and executive director for ASIM, Dr Boyle was chairman for the Health Agenda for the American People, a three-year study on health policy. A knowledgeable and captivating speaker, Dr Boyle brings to the forum the perspective of physicians and the challenges they will face in the modern medical marketplace.

Computer Seminars Friday, September 27, 1985 9:00 a.m.-5:00 p.m.

The USMA computer seminars will provide cutting-edge information for physicians who are potential, new or experienced users.

Scientific Program Friday, September 27, 1985 9:00 am-12:00 Noon

This exceptional half-day course provides a medical update on heart and vascular disease.

Private Practice Marketing Strategies Friday, September 27, 1985 1:30-4:30 pm

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ACADEMIC GENERAL INTERNISTS, CARDIOLOGIST, AND ENDOCRINOLOGIST, DO—Wanted for full-time faculty positions. Must be Board admissible or certified, interested in teaching medical students and house staff. Good balance between clinical practice and teaching with research opportunities available. Assistant Professor level with excellent guaranteed salary and benefits. Send CV to Victor H. Kaylarian, DO, Department of Medicine, University of Osteopathic Medicine and Health Sciences, 3200 Grand Ave., Des Moines, IA 50312. All inquiries confidential.

GENERAL/ORTHOPEDIC SURGEON/FP/-INTERNIST to join multispecialty group in New Mexico. Excellent benefit package. First year salary guarantee negotiable. Well-equipped private outpatient clinic. Five minutes from new hospital. Call Mr. Miller or write 114 West 11th St., Silver City, NM 88061; (505) 388-1511, or (505) 538-2408 in evenings.

NORTHERN CALIFORNIA: Physician, Board certified/eligible in Emergency Medicine or Family Practice, to work part-time or full-time in busy free-standing emergency center. Competitive compensation and malpractice paid. Send CV and references to Joanne Berkowitz, MD, The Emergency Center Medical Group, 4948 San Juan Ave., Fair Oaks, CA 95628.

IMMEDIATE OPENING—Opportunity for Internist, Cardiologist or Family Practice to join two doctor clinic grossing near $400,000. Opportunity to buy in also. Two Surgeons and over five Family Practice Doctors who will support an Internist. Central WA; (509) 422-2600.

CALIFORNIA—Board Certified/eligible or residency trained emergency physician wanted to join 320 physician multispecialty group. Competitive salary and excellent fringe benefits. Ninety miles from Sierra skiing and San Francisco. California license required. Send curriculum vitae to Mrs. Carolyn Whelan, The Permanente Medical Group, Inc., PO Box 254999, Sacramento, CA 95825. An equal opportunity employer.

CALIFORNIA, RURAL AMERICAN AND OVERSEAS: Primary care physicians and OB/GYN needed for locum and permanent placements in CA, Saudi Arabia and, southwestern US. Excellent financial package, practice management and affiliation with a dynamic healthcare company. CV to: Beverly Froley, Westworld Healthcare Resources, 23832 Rockfield Rd., Lake Forest, CA 92630; (800) 847-1596.

EMERGENCY PHYSICIAN, San Francisco Bay Area. Leading HMO seeking ABEM certified/residency trained Emergency Physician or Internist with extensive emergency medicine experience for full-time position. Competitive salary with outstanding benefits leading to shareholdership. Send CV to J. A. McCowin, MD, Emergency Dept., Permanente Medical Group, 280 W. MacArthur Blvd., Oakland, CA 94611, or call (415) 428-5634.

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SOUTHERN CALIFORNIA

Prestigious HMO is seeking experienced specialists and general practitioners for our facilities in Los Angeles and Orange Counties. Located in close proximity to major teaching centers, we offer the opportunity for continued professional development and rewarding clinical practice. Excellent compensation and benefits including paid malpractice, life, disability, medical and dental coverage, paid vacations, sick leave, educational leave and retirement plan. Please send CV to: Director/Physician Recruitment, CIGNA Healthplans of California, 700 North Brand Blvd., Suite 500-49, Glendale, CA 91203.

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GENERAL INTERNAL MEDICINE SPECIALIST position open with 35 member multispecialty group. Excellent practice opportunity, full range of benefits, immediate shareholder status, all practice costs paid. For more information contact: Colin Wells, MD, Recruitment Coordinator, or David E. Graham, Associate Administrator, San Luis Medical Clinic, Ltd., 1235 Osos St., San Luis Obispo, CA 93401; (805) 546-5600.

BOARD CERTIFIED OR ELIGIBLE. Family Practitioner to practice in active county outpatient clinic. Responsibilities to include shared OB, call coverage and inpatient duties. Rural northern California county with 42,000 population, four seasons and excellent local recreational opportunities. The County provides a benefit package which includes vacation, holidays and each occurrence malpractice insurance coverage. Positions may be negotiated as to individual contract or County package. Contact: Dr. Gumm, Medical Director, Tehama County Health Center, 1850 Walnut St., Red Bluff, CA 96080; (916) 527-0350.

2,000 SQUARE FEET office space available for health professional. Area in need of General Practitioner and Internist. Contact Olympic Professional Building, c/o Anita Paves, MD, 193 S. Market Blvd., Chehalis, WA 98532; (206) 748-3366.

CALIFORNIA, NORTHERN: We are seeking career-oriented emergency physicians to staff the emergency department at the new Kaiser Hospital in South Sacramento. Advantages include ideal location midway between San Francisco and the Sierra Nevada Mountains, excellent patient mix, freedom from contract billing hassles, competitive salary, and outstanding fringe benefits. Send CV to William Durston, MD, c/o Mrs. Carolyn Whelan, The Permanente Medical Group, Inc., PO Box 254999, Sacramento, CA 95825. An equal opportunity employer.

INTERNIST, Board certified/eligible to share medical suite, overhead expenses. One-year-old, thriving solo practice in Albuquerque, New Mexico's fastest growing city. Brand new spacious offices. Excellent weather, plenty of recreational opportunities. Send CV to F. Torres, MD, 4801 McMahon Blvd., N.W., Suite #250, Albuquerque, NM 87120.

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FACULTY MEMBER OF COMP looking for associate interested in structural rehabilitation. Opportunity to build an exciting practice at a large preventive medical clinic with DOs and MDs in beautiful La Jolla, California. Opening immediately. For information, contact Ruth I. Gotsch, DO, 8950 Villa La Jolla Dr., Suite 2162, La Jolla, CA 92037; (619) 457-1314.

CALIFORNIA, SONOMA COUNTY—B/C or B/E FP to associate with B/C FP in growing community 60 minutes north of San Francisco. Salary or percentage to start. Hours negotiable. Contact Thomas H. Moore, DO; (707) 795-4560.

OTOLARYNGOLOGIST with interest or fellowship in Otology (BC/BE) to join 40-physician multispecialty group in California. Well-equipped office, salary plus incentive, excellent benefits, location. Send résumé to Box 6493, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

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PSYCHIATRIST—Board eligible, half-time salaried inpatient position with county/private patients. Private practice inpatient/outpatient available. Bilingual in Spanish preferred. Apply to Owen Lum, MD, Dominican Santa Cruz Hospital Mental Health Unit, 1555 Soquel Dr., Santa Cruz, CA 95060; or call (408) 476-0220, Ext. 1400.

PULMONOLOGIST, Boarded Internal Medicine and Board eligible Pulmonology, to join 35-member multispecialty group located on the California central coast. Premium location, excellent practice opportunity with fully paid benefit and retirement program; guaranteed salary first six months followed by incentive pay program; all practice costs paid. For more information contact: Colin Wells, MD, Recruitment Coordinator, or David Graham, Associate Administrator, San Luis Medical Clinic, Ltd., 1235 Osos St., San Luis Obispo, CA 93401; (805) 546-5600.

TWO FULL-TIME FACULTY POSITIONS available in the Department of Family Practice, University of California, Davis; level of appointment commensurate with academic experience and credentials. Should be Board certified by the American Board of Family Practice with interest, training, and/or experience in teaching, research and academic publication activities. These positions will remain open until filled . . . applications will not be accepted after 12/31/85. Send CV to Robert C. Davidson, MD, Chair, Department of Family Practice, University of California, Davis, 2221 Stockton Blvd., Sacramento, CA 95817. The University of California is an affirmative action, equal opportunity employer.

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(Continued on Page 422)

(Continued from Page 420)

PHYSICIANS WANTED

PEDIATRICIAN: Immediate opening for Board eligible/certified Pediatrician with the Western Montana Clinic in an outstanding university town of 30,000 with excellent practice, recreational, and educational opportunities. Contact: Wesley W. Wilson, MD, Western Montana clinic, 515 West Front St., Missoula, MT 59802.

CALIFORNIA, SAN FRANCISCO BAY AREA: Full-time career Emergency Physician wanted for high volume Emergency Department. Emergency Medicine Board certified or Board-ready mandatory to participate in a group of twenty full-time staff physicians seeing over 300 patients per day. Salaried position, excellent benefits include three weeks paid vacation; one week CME; paid malpractice, health and life insurance; corporate shareholdership in three years. Send CV or contact William Green, MD, or David Gallagher, MD, 27400 Hesperian Blvd., Hayward, CA 94545.

SEATTLE, WASHINGTON: Progressive multispeciality group, University affiliated, seeks BC/BE Family Practitioner to join developing family medicine service. Comprehensive primary care, including obstetrics. Excellent salary, benefits. Contact: Ms Y. Westover, (206) 324-5676, Pacific Medical Center, 1200 12th Ave. So., Seattle, WA 98144.

SANTA BARBARA, CA—Internist, Board certified/eligible, energetic General Internist to join well-established group of rehabilitation physicians in beautiful coastal city to provide internal medicine care for 46 bed freestanding hospital specializing in treatment of physical disabilities, e.g., strokes, spinal cord injuries, traumatic head injuries, amputees. Salary negotiable. Contact: Martin Wice, MD, Box 3098, Santa Barbara, CA 93130.

NONINVASIVE CARDIOLOGIST with interest in electrophysiology for the opportunity to practice noninvasive cardiology with a well-established practice. Duties include: supervising and interpreting treadmills, 24-hour monitors, 2D and M-Mode echocardiography, exams and hospital rounds. Excellent salary, plus benefits. Located in central California, Immediate opening. Reply with CV to Box 6492, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

WESTERN WASHINGTON—Private practice openings in Family Practice, Internal Medicine, Pulmonary, OB/GYN, and Otolaryngology. For information, please call Eloise Gusman, 1 (800) 535-7698; or send CV to 2800 Veterans Blvd., Suite 170, Metairie, LA 70002.

WANTED—FAMILY PRACTICE ASSOCIATE—Pleasant Central California community close to mountains, ocean, San Francisco and Los Angeles. Medical school affiliation possible. Well established general practice with light obstetrics. Salary plus incentive. Available immediately. Woman preferred. Reply to Kathleen A. Baron, MD, 1163 East Warner Ave., Fresno, CA 93710; (209) 432-1700.

TRAUMA SURGEON needed to join established group providing comprehensive trauma care. Send CV to Trauma Surgical Associates, Inc., 25 North 14th St., Suite 780, San Jose, CA 95112.

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OBSTETRICIAN-GYNECOLOGIST—Personable and industrious female Obstetrician-Gynecologist desired to join 3-physician department in 28-physician multispecialty group. Immediate practice opportunity. Drawing area 185,000. Western slope of the Rockies. Excellent hospital facilities. Superb living conditions. Unexcelled skiing and outdoor recreation. Primary fee-for-service. HMO option. Please send curriculum vitae and references to Mary Beard, MD, Ogden Clinic, 4650 Harrison, Ogden, UT 84403.

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WASHINGTON COASTAL COMMUNITY serving a population of 65,000 is actively recruiting the following specialists: Orthopedic Surgeon, Urologist, Otolaryngologist, General Surgeon. A variety of practice support options are available, i.e. office space, relocation assistance, etc. Enjoy the support of major West Coast Catholic Hospital System. Community has close proximity to major recreational areas and easy access to Seattle and Portland. For information send CV and references to: Nancy Friedrich, The Friedrich Group, 9284 Ferncliff N.E., Bainbridge Island, WA 98110.

PHYSICIAN SHORTAGE—Primary Care Physicians needed in Seattle Suburban Community now. In response to community needs, a major full-service hospital is encouraging the development of Primary Care Physician Practices. Commercial financing contracts are being arranged by the hospital. This high-growth, high-employment community has some existing practices available. For more information, please call or write The Friedrich Group, 9284 Ferncliff N.E., Bainbridge Island, WA 98110; (206) 842-5248 or (206) 329-0417.

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PHYSICIANS WANTED

CALIFORNIA: University of California Davis Medical Center, Division of Emergency Medicine. Full-time positions are available for physicians in the Division of Emergency Medicine. We are an academic medical center and the trauma center for a large region of Northern California. The positions are clinical faculty appointments with the University of California Davis School of Medicine and entail direct patient care in the Emergency Department as well as teaching the housestaff and medical students of the University of California Davis Medical Center. Applicants should send curriculum vitae to Robert Derlet, MD, Division of Emergency Medicine, UCDMC, 2315 Stockton Blvd., Trailer 1219, Sacramento, Ca 95817.

FAMILY PRACTITIONER—Full-time position available for residency trained, Board eligible/Board certified Family Practitioners interested in practicing in a comprehensive care environment. Outpatient care and in-hospital responsibilities are offered in a growing family practice organization. Administrative opportunities also available. For information, call William Trainor, Manager Professional Staffing, toll-free 1 (800) 446-2255; in California call 1 (800) 336-2255. FHP Professional Staffing, 400 Oceangate Blvd., Suite 1317, Long Beach, CA 90802. For opportunities in Utah, call Maryalys Poulson, collect, at (801) 355-1234.

PHYSICIAN ASSISTANT (ACUPUNCTURE)

SEND RÉSUMÉ TO: EMPLOYMENT SECURITY DEPARTMENT; ES Division; Attn: AEC 45551; Olympia, WA 98504

JOB DESCRIPTION: Required to perform acupuncture procedures as specifically indicated by supervising physician. Selects needles of various lengths, according to location of insertion, inserts needles at locations of body known to be efficacious to certain disorders, utilizing knowledge of acupuncture points and their functions. Leaves needles in patient for specific length of time, according to symptom or disorder treated and removes needles. Burns bark of mugwort tree in small strainer to administer moxibustion treatment. Covers insertion area with cloth and rubs strainer over cloth to impart heat and assist in relieving patient's symptoms.

REQUIREMENTS: 2 years of training in acupuncture training school or equivalent, plus 2 years of experience in the field. Must be eligible for licensure as Physician Assistant (Acupuncture) in Washington State.

SALARY: $2,738 per month

POSITION OFFERS PREVAILING WORKING CONDITIONS, 40 hours per week, 8 AM to 5 PM, position in Edmonds, WA

ON-THE-JOB TRAINING NOT OFFERED
EQUAL OPPORTUNITY EMPLOYER

LOCUM TENENS

LOCUM TENENS SERVICE
WESTERN PHYSICIANS REGISTRY

. . . offers coverage for vacation or continuing education. To arrange coverage for your practice or to participate as temporary physician, contact: **Carol Sweig, Director, 1124 Ballena, Alameda, CA 94501; (415) 521-4110.**

SAN FRANCISCO BAY AREA part-time physician needed for geriatric community clinic. Unique preventive health setting. Send CV to Over 60 Health Clinic, 1860 Alcatraz, Berkeley, CA 94703 or call (415) 644-6060. Experience in Geriatrics desired.

PRACTICES AVAILABLE

CALIFORNIA BAY AREA. Primary Care for sale. Established General Practice one hour to San Francisco. Area growing very rapidly. $100,000+ gross last 5 years. Asking $50,000 but very flexible, depending on amt. of equip I leave. Please reply Box 6490, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

WELL ESTABLISHED GENERAL PRACTICE and free standing care center in Northern California for sale. Office fully equipped. Inquiries Box 6481, Western Journal of Medicine, 44 Gough St, San Francisco, CA 94103.

CALIFORNIA: Otolaryngology, Pediatric, Psychiatric, Opthalmology, Allergy, OBG, Family, Internal, Surgery, Orthopedic, others. Contact Mary Bradshaw, Practice Broker/Recruiter, 21 Altamount Dr., Orinda, CA 94563; (415) 376-0762.

ORTHOPAEDIC PRACTICE—Orange County, California, adjacent to major hospital; five additional hospitals in 5-mile radius; will aid in transition. Box 4191, Irvine, CA 92714.

SAN FRANCISCO BAY AREA. Established Family Practice with growth potential, low overhead, call group. Reply to Box 6491, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

(Continued on Page 424)

(Continued from Page 422)

PRACTICES AVAILABLE

FAMILY PRACTICE—Marin County, California. Rare opportunity to share office space and call in a community based private practice located 45 minutes north of San Francisco. Respond to Box 255, Fairfax, CA 94930. (415) 485-1415 (during office hours).

PEDIATRIC PRACTICE for sale. Reasonable. Fastest growing San Francisco Bay area. Great potential. Reply Box 6494, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

REAL ESTATE

SAN LEANDRO: Prime, central. Prestige medical building. Ample parking. *Great* opportunity Internist or GP. Carol Bull, (415) 357-8940.

CENTRAL CALIFORNIA Arroyo Grande. Long term leasehold space with option to buy. 2,000+ square feet in new professional complex. Available in October. Help design interior now. Construction allowance given. (213) 649-0036.

SITUATIONS WANTED

PATHOLOGIST—Board certified AP, CP. Twelve years experience. Strong background Surgical Pathology with special interests Hematopathology and Cytopathology. Seeks position as associate in preferably group practice. Western states preferred. Available immediately. B. Swinyer, MD, 7805 Buena Tierra, Bakersfield, CA 93309.

MIDDLE-AGED, VERY ACTIVE Orthopaedic Surgeon, Board certified looking to join a group specialty practice or multispecialty group or join a private practice in vicinity of Los Angeles, Sacramento, or San Diego. Please contact Box 24723, Los Angeles, CA 90025.

OFFICE SPACE AVAILABLE

MEDICAL OFFICE SPACE—Available for lease, 1,008 square feet. Occupied since 1964 by Family Practitioner. In professional office complex situated in Rohnert Park, 50 miles north of San Francisco. Call (707) 795-5485 or write M. Fredericks, 6950 Commerce Blvd., Rohnert Park, CA 94928.

LEGAL COUNSEL

SERVICES

PATIENT NEWSLETTER: Keeping in touch shows that you care! Send for your free sample copy of our quarterly health promotion newsletter. Customized for you. Mailing service option. Rx: Live well, 6809 Santa Maria Ln., Dallas, TX 75214-2847 or call (214) 821-5218.

SERVICES

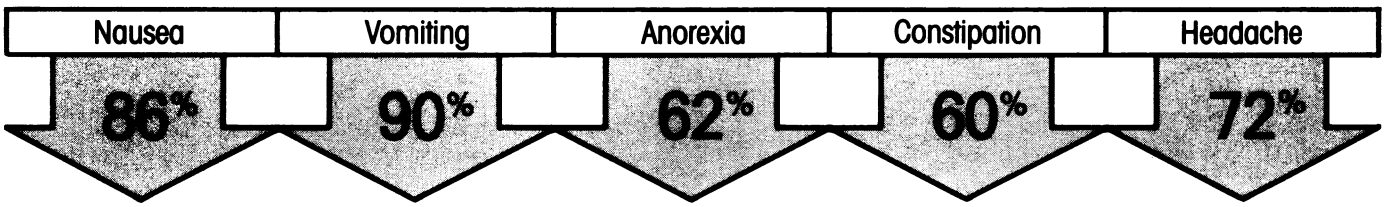
In moderate depression and anxiety

FEELING BETTER FASTER...

OVERNIGHT—SLEEP IMPROVED[1]

Sleep improved in 74% after only one *h.s.* dose in selected patients

FIRST WEEK—OTHER SOMATIC SYMPTOMS MARKEDLY REDUCED[1]



FOURTH WEEK—PATIENT COMPLIANCE WAS BETTER[2]

More than three times as many amitriptyline patients as Limbitrol patients dropped out of therapy because of side effects, although the incidence of side effects was similar. Caution patients against the combined effects of Limbitrol with alcohol or other CNS depressants and about activities requiring complete mental alertness, such as operating machinery or driving a car. In general, limit dosage to lowest effective amount in elderly patients.

References: 1. Data on file, Hoffmann-La Roche Inc., Nutley, NJ. 2. Feighner JP, *et al: Psychopharmacology 61*:217-225, Mar 22, 1979.

Limbitrol®

Each tablet contains 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt) Ⓒ Ⓥ

Limbitrol® DS

Each tablet contains 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt) Ⓒ Ⓥ

A brighter perspective...sooner

Limbitrol® Ⓒ Ⓥ Tranquilizer–Antidepressant

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of moderate to severe depression associated with moderate to severe anxiety.

Contraindications: Known hypersensitivity to benzodiazepines or tricyclic antidepressants. Do not use with monoamine oxidase (MAO) inhibitors or within 14 days following discontinuation of MAO inhibitors since hyperpyretic crises, severe convulsions and deaths have occurred with concomitant use; then initiate cautiously, gradually increasing dosage until optimal response is achieved. Contraindicated during acute recovery phase following myocardial infarction.

Warnings: Use with great care in patients with history of urinary retention or angle-closure glaucoma. Severe constipation may occur in patients taking tricyclic antidepressants and anticholinergic-type drugs. Closely supervise cardiovascular patients. (Arrhythmias, sinus tachycardia and prolongation of conduction time reported with use of tricyclic antidepressants, especially high doses. Myocardial infarction and stroke reported with use of this class of drugs.) Caution patients about possible combined effects with alcohol and other CNS depressants and against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving).

***Usage in Pregnancy:* Use of minor tranquilizers during the first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Since physical and psychological dependence to chlordiazepoxide have been reported rarely, use caution in administering Limbitrol to addiction-prone individuals or those who might increase dosage; withdrawal symptoms following discontinuation of either component alone have been reported (nausea, headache and malaise for amitriptyline; symptoms [including convulsions] similar to those of barbiturate withdrawal for chlordiazepoxide).

Precautions: Use with caution in patients with a history of seizures, in hyperthyroid patients or those on thyroid medication, and in patients with impaired renal or hepatic function. Because of the possibility of suicide in depressed patients, do not permit easy access to large quantities in these patients. Periodic liver function tests and blood counts are recommended during prolonged treatment. Amitriptyline component may block action of guanethidine or similar antihypertensives. When tricyclic antidepressants are used concomitantly with cimetidine (Tagamet), clinically significant effects have been reported involving delayed elimination and increasing steady state concentrations of the tricyclic drugs. Concomitant use of Limbitrol with other psychotropic drugs has not been evaluated; sedative effects may be additive. Discontinue several days before surgery. Limit concomitant administration of ECT to essential treatment. See Warnings for precautions about pregnancy. Limbitrol should not be taken during the nursing period. Not recommended in children under 12. In the elderly and debilitated, limit to smallest effective dosage to preclude ataxia, oversedation, confusion or anticholinergic effects.

Adverse Reactions: Most frequently reported are those associated with either component alone: drowsiness, dry mouth, constipation, blurred vision, dizziness and bloating. Less frequently occurring reactions include vivid dreams, impotence, tremor, confusion and nasal congestion. Many depressive symptoms including anorexia, fatigue, weakness, restlessness and lethargy have been reported as side effects of both Limbitrol and amitriptyline. Granulocytopenia, jaundice and hepatic dysfunction have been observed rarely.

The following list includes adverse reactions not reported with Limbitrol but requiring consideration because they have been reported with one or both components or closely related drugs:

Cardiovascular: Hypotension, hypertension, tachycardia, palpitations, myocardial infarction, arrhythmias, heart block, stroke.

Psychiatric: Euphoria, apprehension, poor concentration, delusions, hallucinations, hypomania and increased or decreased libido.

Neurologic: Incoordination, ataxia, numbness, tingling and paresthesias of the extremities, extrapyramidal symptoms, syncope, changes in EEG patterns.

Anticholinergic: Disturbance of accommodation, paralytic ileus, urinary retention, dilatation of urinary tract.

Allergic: Skin rash, urticaria, photosensitization, edema of face and tongue, pruritus.

Hematologic: Bone marrow depression including agranulocytosis, eosinophilia, purpura, thrombocytopenia.

Gastrointestinal: Nausea, epigastric distress, vomiting, anorexia, stomatitis, peculiar taste, diarrhea, black tongue.

Endocrine: Testicular swelling and gynecomastia in the male, breast enlargement, galactorrhea and minor menstrual irregularities in the female, elevation and lowering of blood sugar levels, and syndrome of inappropriate ADH (antidiuretic hormone) secretion.

Other: Headache, weight gain or loss, increased perspiration, urinary frequency, mydriasis, jaundice, alopecia, parotid swelling.

Overdosage: Immediately hospitalize patient suspected of having taken an overdose. Treatment is symptomatic and supportive. I.V. administration of 1 to 3 mg physostigmine salicylate has been reported to reverse the symptoms of amitriptyline poisoning. See complete product information for manifestation and treatment.

Dosage: Individualize according to symptom severity and patient response. Reduce to smallest effective dosage when satisfactory response is obtained. Larger portion of daily dose may be taken at bedtime. Single *h.s.* dose may suffice for some patients. Lower dosages are recommended for the elderly.

Limbitrol DS (double strength) Tablets, initial dosage of three or four tablets daily in divided doses, increased up to six tablets or decreased to two tablets daily as required. Limbitrol Tablets, initial dosage of three or four tablets daily in divided doses, for patients who do not tolerate higher doses.

How Supplied: *Double strength (DS) Tablets,* white, film-coated, each containing 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt), and *Tablets,* blue, film-coated, each containing 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt). Available in bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 50.

ROCHE

ROCHE PRODUCTS INC.
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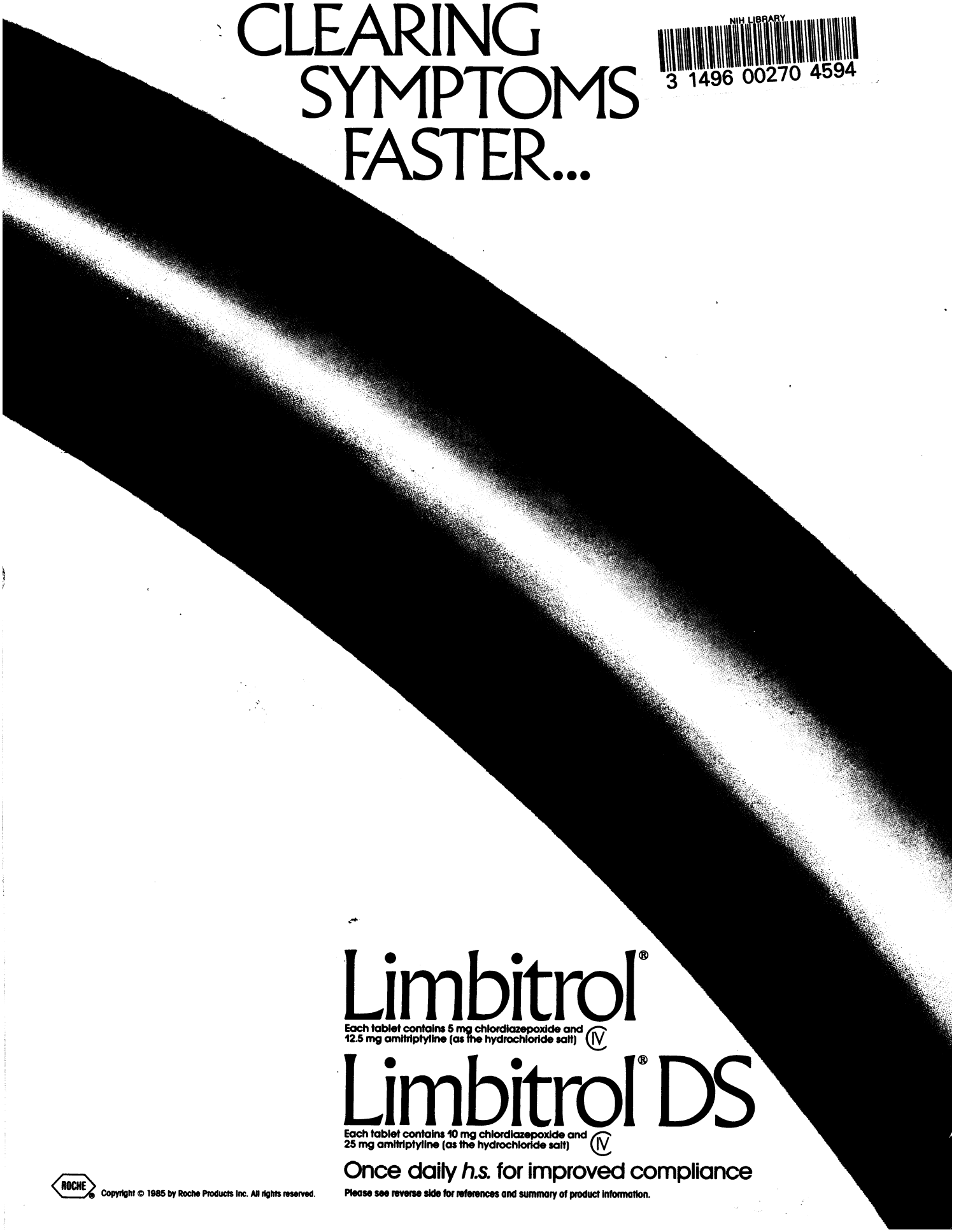
In depression and anxiety

CLEARING SYMPTOMS FASTER...



Limbitrol®

Each tablet contains 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt) Ⓒ Ⓥ

Limbitrol® DS

Each tablet contains 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt) Ⓒ Ⓥ

Once daily *h.s.* for improved compliance

Please see reverse side for references and summary of product information.